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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,408	02/21/2002	Lars Abrahmsen	13425-053001	1557

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	8

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,408	ABRAHMSEN ET AL.	
	Examiner	Art Unit	
	Yong Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,15 and 17-24* is/are rejected.

7)☒ Claim(s) *14 and 16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-26 are pending.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-24) in Paper No. 7 is acknowledged.

Claims 25-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10, 15, 17-19 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. in view of Huston et al. and Tudyka et al.

Smith et al. (form PTO-1449) teach an amino oxidase that is 100% identical to the semicarbazide-sensitive amino oxidase (SSAO) of SEQ ID NO:2 of the instant invention (Figure 1, page 20 and SwissProt sequence alignment). Smith et al. teach that the transmembrane domain is between residues 5-27 (Figure 1, page 20 and page 21) and that the cytoplasmic domain is residues 1-5 (SwissProt). Art and the specification teach that the soluble from of SSAO lacks the membrane spanning portion of the wild-type SSAO.

The difference between the reference of Smith et al. and the instant invention is that the reference of Smith et al. does not teach a DNA molecule encoding a secreted fusion protein comprising a signal peptide, a fusion partner and a protease cleavage site.

Huston et al. (U.S. Patent No. 5,013,653) teach a method of making DNA encoding a fusion protein comprising a signal peptide, a fusion partner to the target protein and a protease cleavage site between the fusion partner and to the target protein (Column 1). Huston et al. teach that a signal peptide can be used in order to protect the target protein from intracellular degradation during expression or isolation/purification(Column 1). Huston et al. also teach that a DNA encoding a

protease cleavage site can be incorporated between the DNA encoding the target protein and the DNA encoding the additional fused material (column 1 and 2). Huston et al. also teach a vector comprising said DNA, a method of producing the target protein and a method of immobilizing the fused target protein (Column 2 and Examples 1-4).

Tudyka et al. (form PTO-1449) teach that GST can be used as a fusion partner that enables dimerization of a target recombinant protein and confers enzymatic reporter activity (abstract and page 2180). Tudyka et al. teach that glutathione S-transferase (GST) from Schistosoma that is 100% identical to the GST of SEQ ID NO:4 of the instant invention. Tudyka et al. teach that replacing three of the four exposed cysteine residues in GST (residues 85, 138 and 178) prevents formation of wrong crosslink formations (abstract and Figure 2-B, page 2182) and the resulting GST mutant is 100% identical to SEQ ID NO:5 of the instant invention. Tudyka et al. also teach that the fusion protein was purified by means of an affinity column with glutathione (abstract) and the GST protein can be proteolytically removed after the fusion protein is produced in the cytoplasm (page 2185).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a DNA molecule encoding a fusion protein comprising a signal peptide, a fusion partner, the GST of Tudyka et al., a target protein, the soluble form of SSAO of Smith et al., and a protease cleavage site between the fusion partner and to the target protein, as outlined by Huston et al. The motivation of making such a fusion construct is to facilitate the protection, isolation and purification of the target protein. The motivation of truncating the transmembrane domain of SSAO

is to produce soluble SSAO, thereby increasing the efficiency of the purification process. The motivation of using the GST of Tudyka et al. is to enable dimerization of SSAO and confers enzymatic reporter activity. The motivation of using the mutant GST of Tudyka et al. is to prevents formation of wrong crosslink formations. One of ordinary skill in the art would have had a reasonable expectation of success since the individual proteins incorporated into the fusion proteins are well known and used in the art and fusion proteins comprising a signal peptide, a target protein, any additional fused material and a cleavage site in between the target protein and the fusion partner outlined by Huston et al. are well known and used widely in the art.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. in view of Huston et al. and Tudyka et al. as applied to claims 1-10, 15, 17-19 and 24 above, and further in view of Zambidis et al.

The reference of Smith et al., Huston et al., and Tudyka et al. in combination teach a DNA encoding a fusion protein comprising a signal peptide, a soluble SSAO, a GST and protease cleavage site, vector comprising said DNA, a method of producing said fusion protein and a method of immobilizing said fusion protein, as discussed above.

The difference between the references and the instant invention is that the combined teachings of the references do not teach a fusion comprising a mouse IgG1 heavy chain signal peptide.

Zambidis et al. teach a mouse IgG1 heavy chain signal peptide (abstract). It is well known in the art that immunoglobulins or IgG proteins facilitate expression of fusion recombinant proteins (Sakurai, page 382 – form PTO 1449).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a DNA molecule encoding a fusion protein comprising a mouse IgG signal peptide. The motivation of making such a fusion construct is to facilitate the expression and purification of the target protein. One of ordinary skill in the art would have had a reasonable expectation of success since IgG1 or other immunoglobulin proteins are well known and well practiced in the art in facilitating expression of heterologous proteins.

Claims 12-13 and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. in view of Huston et al. and Tudyka et al. as applied to claims 1-10, 15, 17-19 and 24 above, and further in view of Brenda Enzyme Database.

The reference of Smith et al., Huston et al., and Tudyka et al. in combination teach a DNA encoding a fusion protein comprising a signal peptide, a soluble SSAO, a GTS and protease cleavage site, vector comprising said DNA, a method of producing said fusion protein and a method of immobilizing said fusion protein, as discussed above.

The difference between the references and the instant invention is that the combined teachings of the references do not teach a fusion comprising a 3C protease of SEQ ID NO:6, 3C protease or a rhinovirus 3C protease.

Brenda Enzyme Database (EC 3.4.22.28 – form PTO-892) teach a 3C protease from Coxsackievirus that is 100% identical to SEQ ID NO:6 of the instant invention. The Database also teaches a picornvirus 3C protease and a rhinovirus 3C protease (pages 3-4). There are many types of protease cleavage sites and 3C proteases is one of the many enzymes capable safely cleaving a fusion partner from the target protein.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a DNA molecule encoding a fusion protein comprising any of the 3C proteases listed in the Brenda Enzyme Database. The motivation of incorporating a cleavage site between the SSAO and GST is to cleave off the GST protein after the fusion protein is produced in the cytoplasm. One of ordinary skill in the art would have had a reasonable expectation of success since 3C proteases are well known enzymes and have been widely used in cleavage sites between target proteins and additional fused material.

Allowable Subject Matter

Claims 14 and 16 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on 6:30 A.M. to 3:30 P.M weekdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong Pak
Patent Examiner

May 29, 2003

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
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